

## REMARKS

The following remarks are offered in complete response to the Office Action dated January 7, 2011. In light of these remarks, reconsideration of the rejections and examination of all of the claimed subject matter on the merits are respectfully requested.

Claims 11-27 are pending in this application. Claim 1-8 have been cancelled. Claims 9 and 10 were previously cancelled. Claims 23-27 have been added.

Claims 16, 17 and 22 are allowed. Claims 11-13 and 15 have been withdrawn from consideration.

Claims 13 and 14 have been amended to recite a method for treating an animal or a human patient having a neurodegenerative disease responsive to treatment with an anti-prion agent, the method comprising administering to said animal or said human patient a composition of claim 16 (claim 13) or 17 (claim 14) and to delete the chemical structure of the compound. The structure of the compounds is recited in claim 16 or 17, from which these claims depend. Support for this amendment is found in the specification at least on page 9, line 19 - page 10, line 25, page 12, lines 21-30, and Example 9, starting on page 29, line 30. Claims 15, 19 and 21 have been amended to include Parkinson's disease in the group of neurodegenerative disease. Support for this amendment is found in the specification at least on page 12, lines 25-26. Claim 15 has also been amended to depend from claim 13 and to recite the diseases in a Markush group. Claims 18 and 20 have been amended to properly recite a method claim and to clarify the condition being treated. Claims 19 and 21 have been amended to delete redundant claim language and to recite the diseases in a Markush group.

New claims 23-25 are analogous to claims 13, 18 and 19 but dependent from claim 22. New claims 26 and 27 are analogous to claim 15, but dependent from claim 14 and 22.

No new matter has been introduced as a result of the foregoing amendments.

Applicant gratefully acknowledge the Examiner's indication that claims 16, 17 and 22 are allowable and that claims 14 and 18-21 are no longer withdrawn from consideration.

**Claim Objections**

Claim 14 is objected to for depending from withdrawn claim 13.

Claim 14 has been amended to incorporate the subject matter of claim 13.

Applicant therefore requests that this objection be withdrawn.

**35 U.S.C. §112 second paragraph Rejection**

Claims 14 and 18-20 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

The Office Action indicates that the patient population(s) of claims 14 and 18-20 is not clearly defined in the claims.

The Office Action states that for Claim 14, "the active method step of the claim is not so linked to the preamble of the claim so as to clearly and unequivocally convey that the administration is to a subject having a neurodegenerative disease."

Claim 14 have been amended to recite in the preamble that the animal or human patient has a neurodegenerative disease and the active step recites "administering to said animal or said human patient a composition of claim 17." The use of the term "said animal or said human patient" clearly and unequivocally conveys that the administration is to a subject having a neurodegenerative disease. Therefore amended claim 14 particularly points out and distinctly claims the subject matter which the applicant regards as the invention.

Applicant therefore requests that this rejection of claim 14 be withdrawn.

With regard to claims 18-21, the Office Action states that the method does not define what is being treated and it is not clear whether the "patient in need thereof" is a patient in need of "treatment" or any patient "in need of" the composition of claim 16.

Claims 18 and 20 have been amended to recite that the method is for the treatment of a neurodegenerative disease and that the composition is being administered for the treatment of that neurodegenerative disease. Therefore amended claims 18 and 20, and claims 19 and 21, which depend from claims 18 and 20, particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

Applicant therefore requests that this rejection of claims 18-21 be withdrawn.

**35 U.S.C. §112 first paragraph Rejection**

Claims 14 and 18-20 have been rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement.

The Office Action alleges that the specification fails to teach one skilled in the art how to make and use the full scope of the invention without undue experimentation. The Office Action cites the various factors outlines in *In re Wands* and provides and focuses on the unpredictability of the art. (pages 4-10).

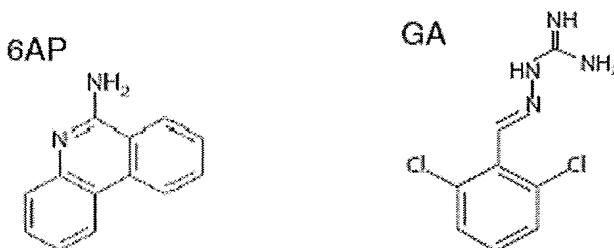
Enclosed are four literature articles that show in vivo activity of anti-prion compounds which were identified using the screening methods described in the specification.

The first paper "Isolation of drugs active against mammalian prions using a yeast-based screening assay" by Bach et al. (Nature Biotechnology 21 (9) 2003) demonstrates that quinacrine and chlorpromazine, two compounds with known anti-prion activity, were active in the yeast-based screening assay and were also active in test system using mammalian cells. (see page 1079, left column, last three paragraphs).

The second paper "Using budding yeast to screen for anti-prion drugs" by Tribouillard et al. (Biotechnology Journal) 2006, 1, 58-67) describes the evaluation of compounds identified as being most active in the yeast assays for anti-mammalian prion activity using various mammalian cell assays. (see Sections 2.5 and 2.6 on pages 64-65) These assays used murine neuroblastoma cells, kidney epithelial cells from a rabbit, cells that replicate a sheep prior strain and murine peripheral neuroglial cells.

The third paper "Antihypertensive Drug Guanabenz is Active *In Vivo* against both Yeast and mammalian Prion" by Tribouillard-Tanvier et al. (PLoS One April 2008, 3(4)) describes the isolation and activity of Guanabenz (GA), a drug used in antihypertensive therapy. The paper describes the *in vivo* activity of guanabenz using a mouse model for prion-based disease where animals were treated at different stages of the disease. The paper concluded "Overall, we have shown in two independent experiments a significant effect of GA on the survival time of mice, in a model that might be difficult to cure, due to the high infectious load inoculated." (see page 4, right column, first paragraph above Discussion).

The fourth paper "Antiprion drugs 6-aminophenanthridine and guanabenz reduce PABPN1 toxicity and aggregation in oculopharyngeal muscular dystrophy" by Barbezier et al. (EMBO Molecular Medicine 3, 35-49) describes the effect of 6AP and GA in *ex vivo* cellular tests, in an *in vivo* murine model for prion disease and an *in vivo* drosophila model for OPMD.



OPMD is a myodegenerative disease associated with the formation of amyloid fibers by the PABN1 protein in the core of muscle cells. This disease is an amyloid fiber disease which is similar to prion disease such as Alzheimer, Parkinson or Huntington diseases.

Applicant is required to follow the rules outlined in the European Directive CEE 86/609, in which experimentation in animals "shall not be performed if another scientifically satisfactory method of obtaining the results sought, not entailing the use of an animal, is reasonably and practicably available." (Article 7.2) Applicant respectfully submits that the use of the *in vitro* testing is a scientifically satisfactory method of obtaining the results sought.

One of ordinary skill in the art would not have been required to perform undue experimentation. The claims are limited to a small number of very closely related compounds. One of ordinary skill in the art is familiar with various routine tests that

could be conducted on such compounds to show their claimed use. In fact, as shown above, positive results were observed in various models using mammalian cells, as well as a murine model. Therefore, the specification enables one of ordinary skill in the art to use the claimed invention.

While the Office Action cites *In re Buting* for showing that human testing "limited to one compound and two types of cancer" was not "commensurate with the broad scope of utility asserted and claimed", the claims of the current application differ in that only a handful of very closely related compounds and a few closely related conditions are claimed in this case, while in *In re Buting* a wide number of different conditions - leukemias, sarcomas, adenocarcinomas, lymphosarcomas, melanomas, myelomas and ascitic tumors, were claimed.

The Office Action also cites *Ex parte Jovanovics*. However, *Ex parte Jovanovics* was not a case related to the enablement requirement of 35 U.S.C. §112, first paragraph, but rather to a 35 U.S.C. §101 requirement.

The Office Action also cites *Ex parte Busse*. However, *Ex parte Busse* also was not a case related to the enablement requirement of 35 U.S.C. §112, first paragraph, but rather to a 35 U.S.C. §101 requirement.

While the Office Action further cites *Ex parte Stevens*, the claims of the instant application are distinguished from *Ex parte Stevens* because the examples in *Ex parte Stevens* were admitted by the appellant to be only an "experimental "paper" protocol and that no experiments had actually been done. In the instant case, experimental work was conducted, as shown in the specification. In addition, as shown above, additional experimental work demonstrates that in various tests using mammalian cells, as well as in a murine model, the claimed compounds were effective.

Claims 14 and 18-20 comply with the enablement requirement. Applicants therefore request that this rejection be withdrawn.

From the foregoing, Applicants earnestly solicit further and favorable action in the form of a Notice of Allowance.

**Conclusion**

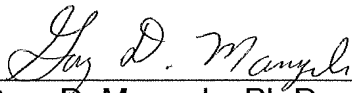
For at least the foregoing reasons, Applicants respectfully request further examination, reconsideration and withdrawal of all outstanding rejections, and formal notification of allowance. If the Examiner perceives any impediment to such formal notification of allowance, whether substantive or merely formal, Applicants encourage the Examiner to telephone their representative at the number provided below. Such informal communication will expedite examination and disposal of the instant case.

The Director is hereby authorized to charge any appropriate fees under 37 C.F.R. §§ 1.16, 1.17 and 1.20(d) and 1.21 that may be required by this paper, and to credit any overpayment, to Deposit Account No. 02-4800.

Respectfully submitted,

BUCHANAN INGERSOLL & ROONEY PC

Date: April 7, 2011

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